

# TRACO – Introduction to Radiation Oncology

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# Disclosures

- Disclosures: None

# Outline

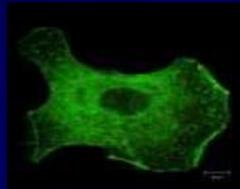
- Goals of cancer therapy
- Goals of radiation therapy
- Basics of radiation oncology
  - Radiation Physics
  - Radiation Biology
  - Radiation Therapy
  - Patient presentations
- The future of radiation oncology

# Principles of cancer therapy

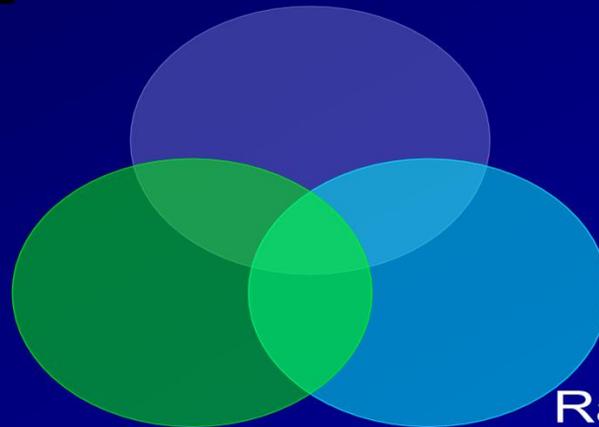
- Minimize therapy
  - Toxicity, time, cost
- Minimize negative impact on quality of life
  - Toxicity, function, cosmesis
- Improve quality of life
  - Palliation, organ preservation
- Maximize impact on quantity of life
  - Cure and remission
- Improve outcomes
  - Research

# Radiation Oncology

The discipline of radiation oncology



Radiation Biology



Physics

$$E=mc^2$$



Radiation Therapy



# The Physics of Radiation Oncology

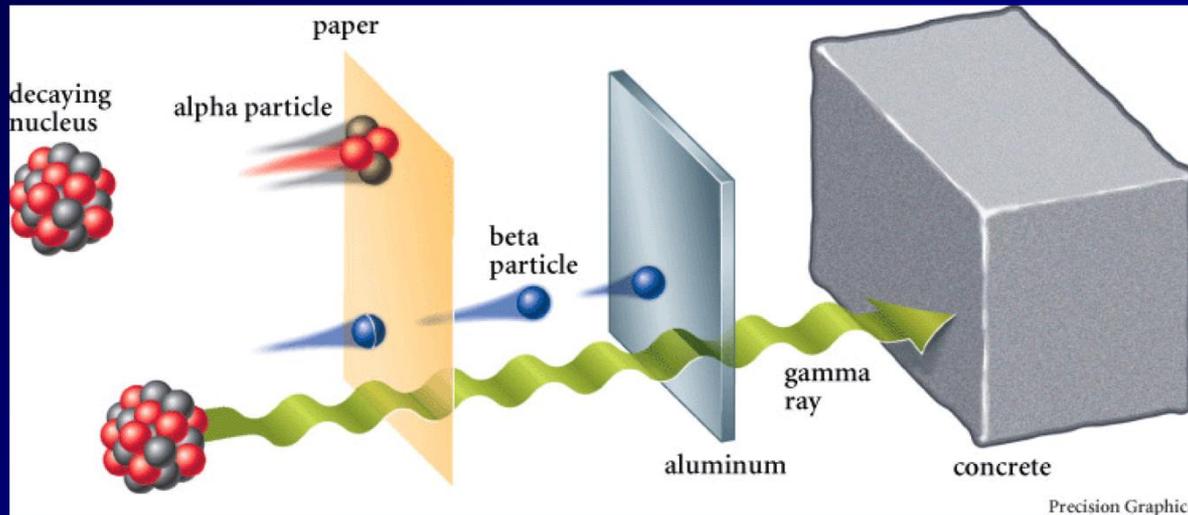
Just the basics

# The Physics of Radiation Oncology

- What is radiation?
  - “the complete process by which energy is emitted by one body, transmitted through an intervening medium or space, and absorbed by another body.”

# Types of Radiation

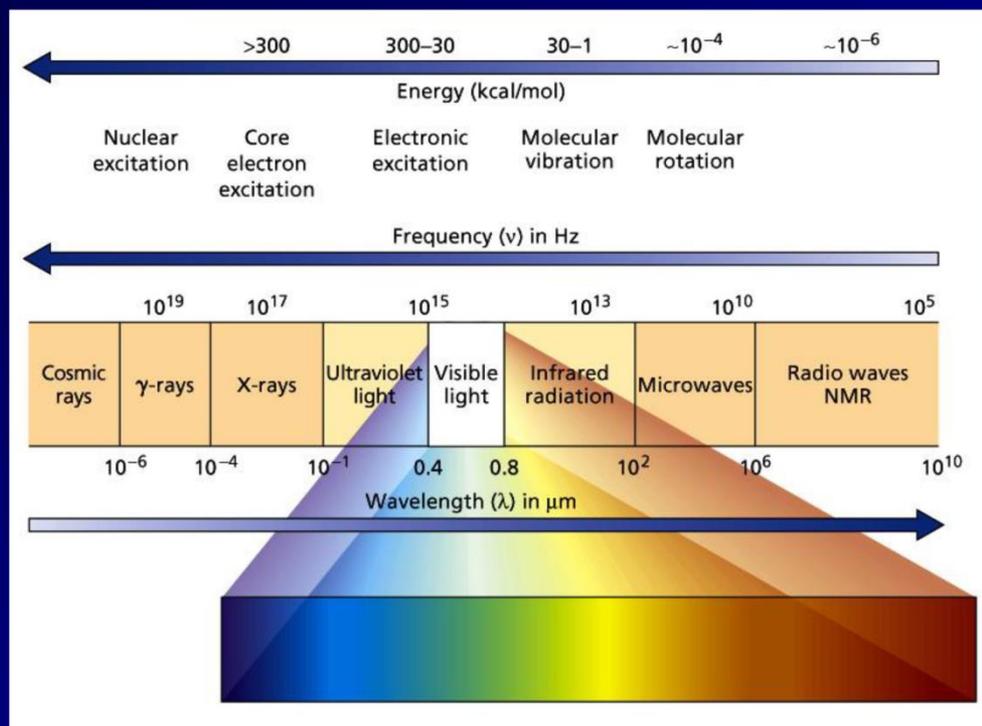
## Types of Radiation



Particles and photons

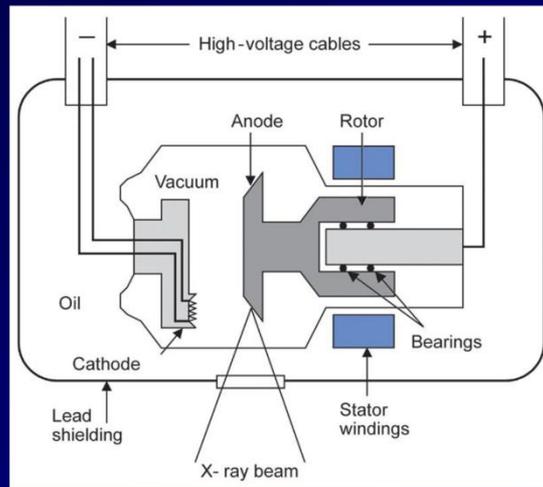
# The Electromagnetic Spectrum

## The electromagnetic spectrum



# X Rays

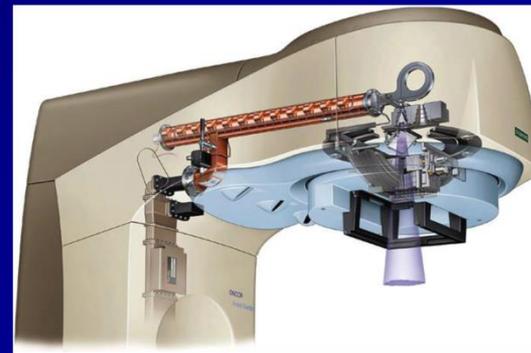
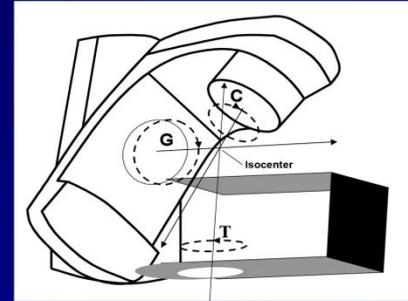
How are x rays generated?



# The Linear Accelerator

## The linear accelerator

- High energy photons and electrons
- Uniform beam characteristics
- Precise field shaping
- Precise delivery
  - The gantry rotates
  - The couch rotates
  - The patient is immobilized



# Radiation therapy basics

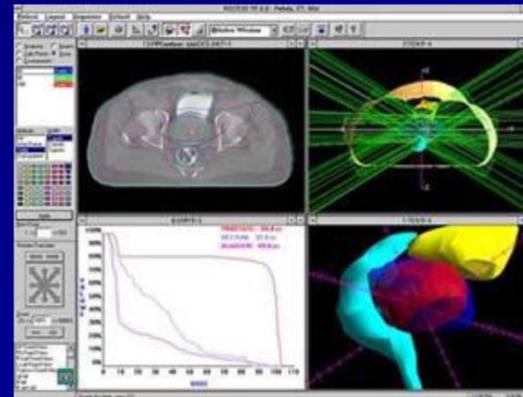
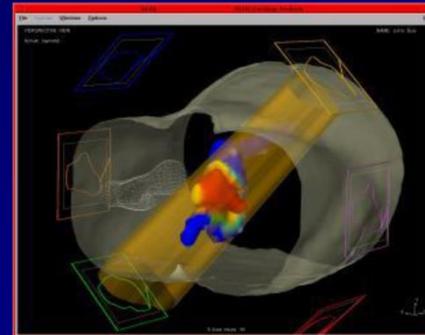
## Radiation Therapy Basics

- GTV = Gross tumor volume
- CTV = Clinical target volume; typically margin added for microscopic extension; may be limited at anatomic boundaries
- PTV = planning target volume; isotropic margin to account for 'set up uncertainty'.
- ITV = internal target/tumor volume; volume drawn accounting for organ or tumor motion

# Radiation Planning Techniques

## Radiation Planning Techniques

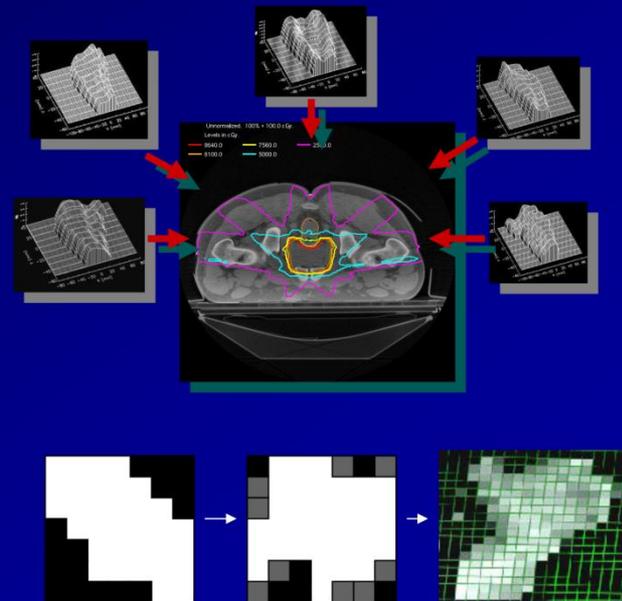
- 3D CRT
  - Use CT to plan from anatomy, allows freedom of multiple angles
  - “Virtual patient”
- IMRT
  - Dose cloud, complex
  - Inverse planning



# Intensity Modulated Radiation Therapy

## Intensity Modulated Radiation Therapy

- Modulation of the intensity across each beam
- Allows customization based on a specific planning objective
  - Treat tumor to 50Gy, keep bladder dose below 20 Gy.



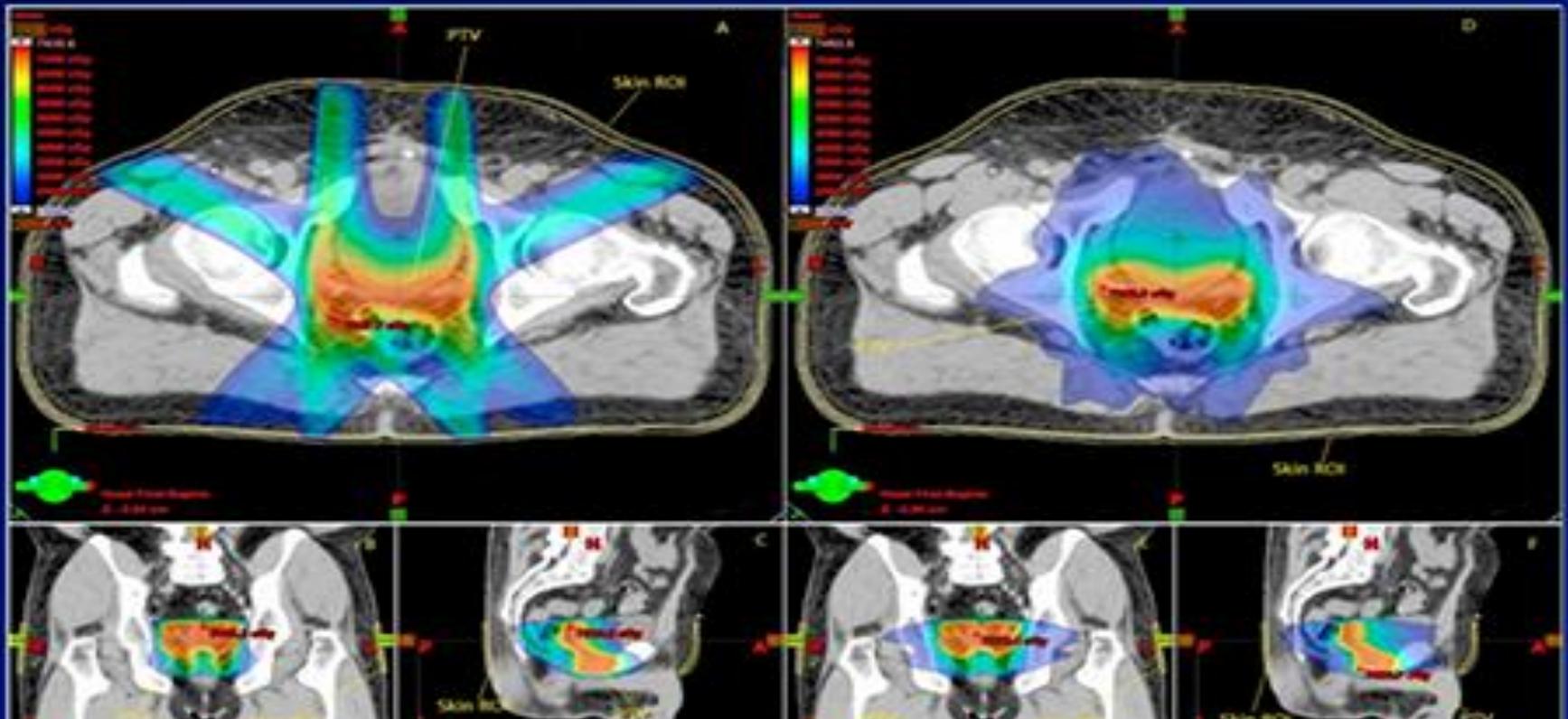
# VMAT

## Volumetric Modulated Arc Therapy (VMAT)

- Linac moves and can deliver dose in 360 arc around patient
- Quicker treatment delivery
- More conformal for moderate dose of prescription
- Improved dose homogeneity
- More low dose to surrounding tissues

# VMAT

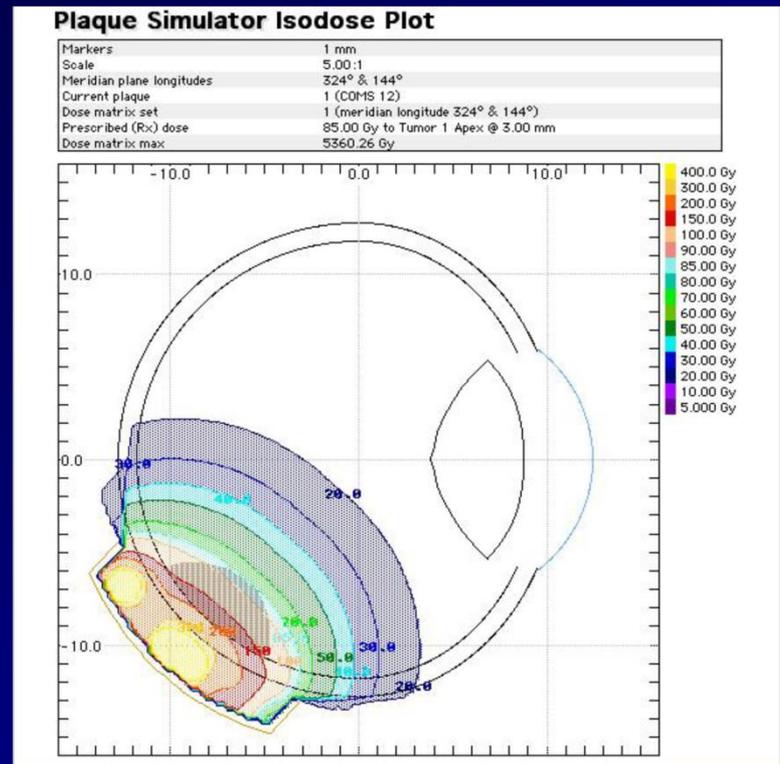
# VMAT



# Brachytherapy

- Placing a radiation source inside or adjacent to the tumor
- Rapid dose fall-off allows maximal sparing of normal tissues (no “going through” normal tissue to get to the tumor)
- Used commonly for tumors
  - in body cavities (cervix, endometrium, vagina, nasopharynx)
  - close to the surface (prostate, sarcoma, tongue, lip, breast)

# Plaque Simulator Isodose Plot

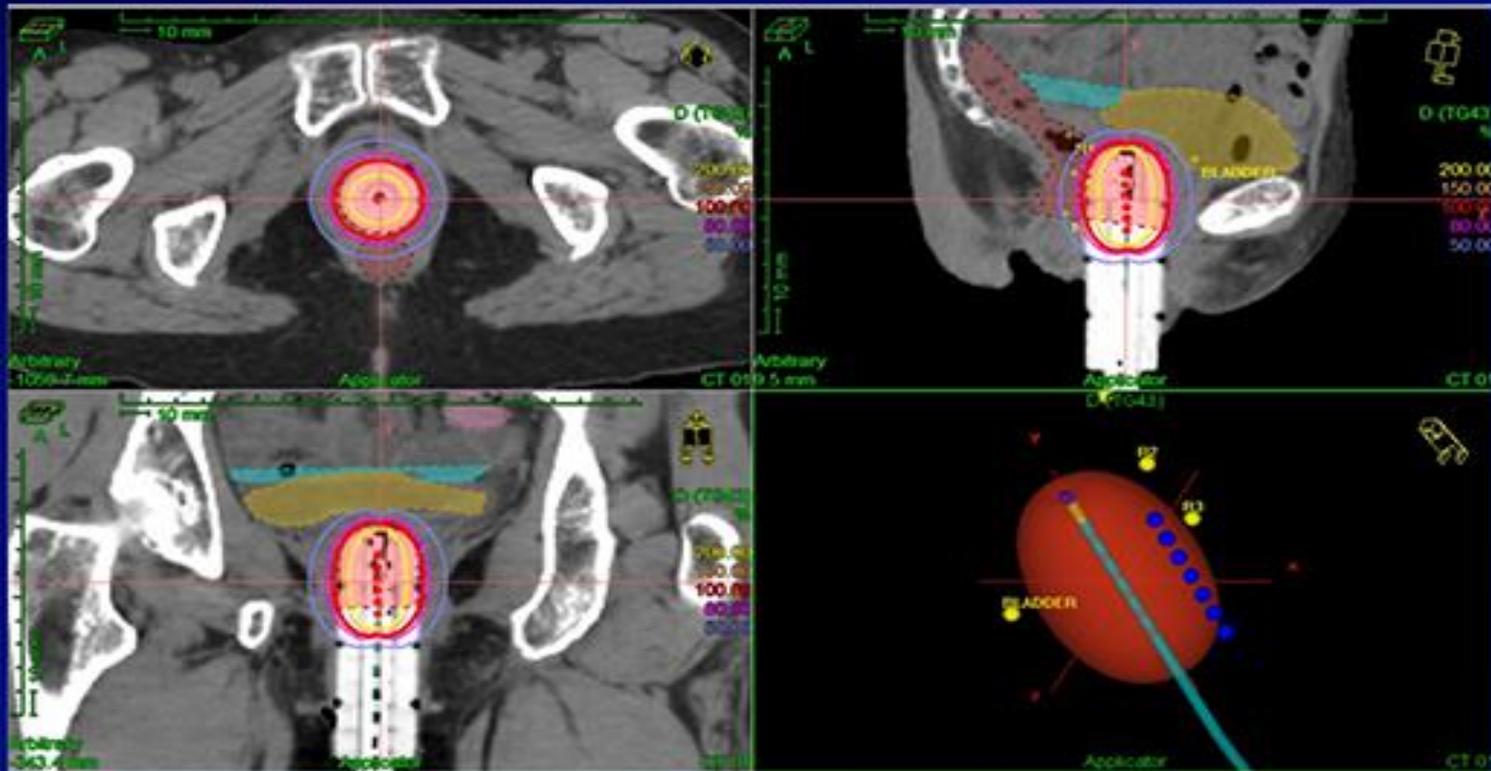


# Brachytherapy

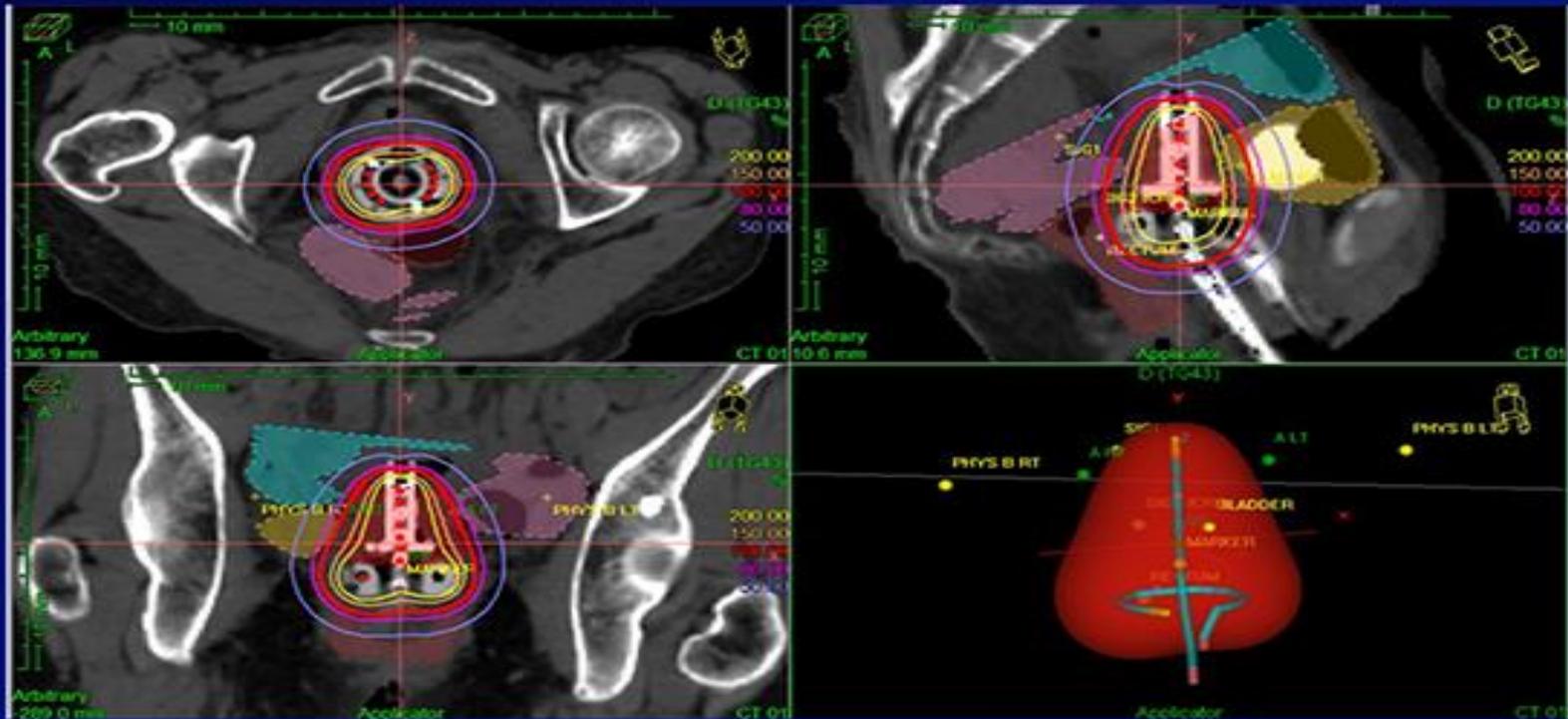
## Brachytherapy

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- Used commonly for tumors
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  - close to the surface (prostate, sarcoma, tongue, lip, breast)
- Delivered with Iridium-192

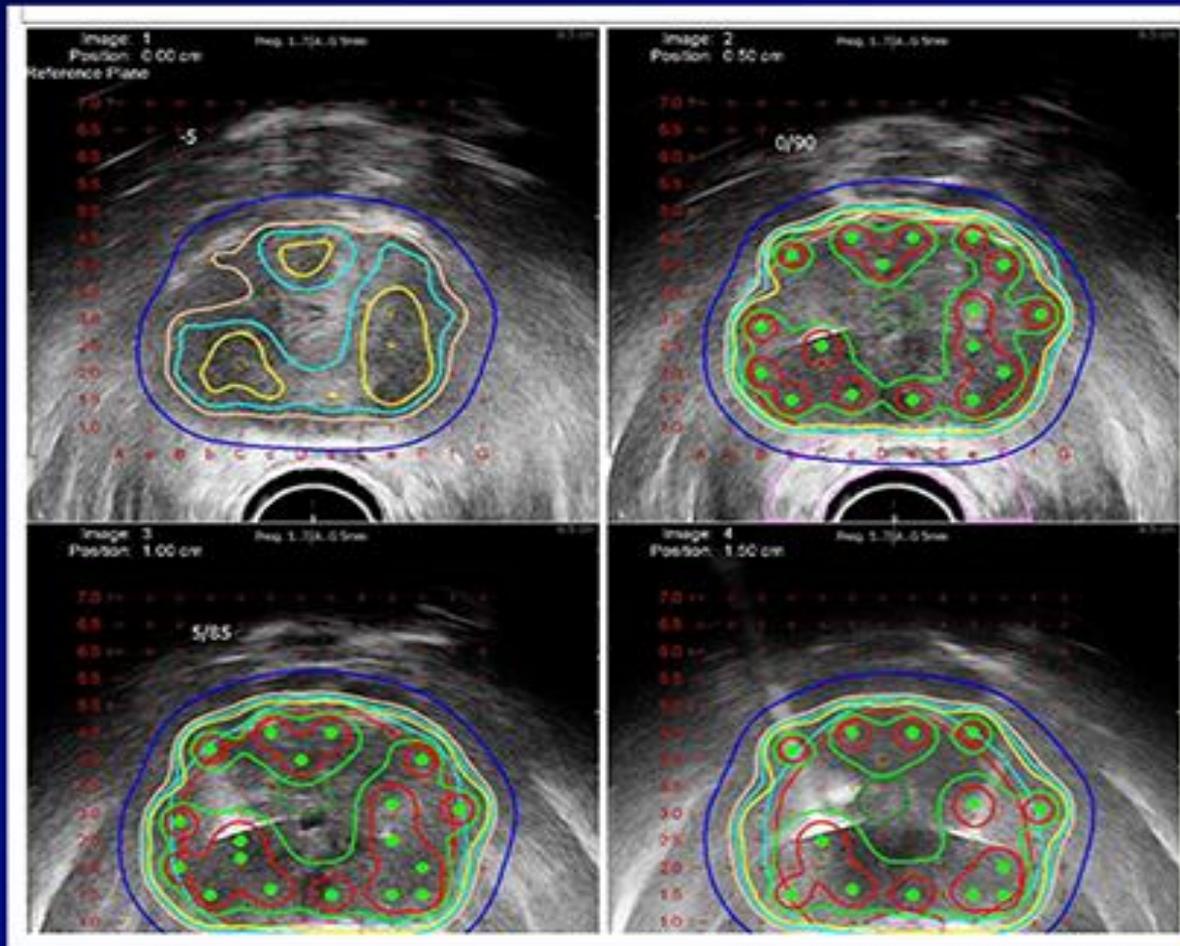
# Brachytherapy



# Brachytherapy



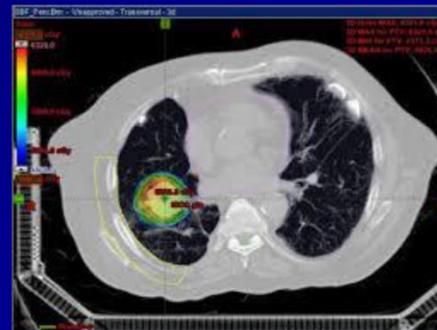
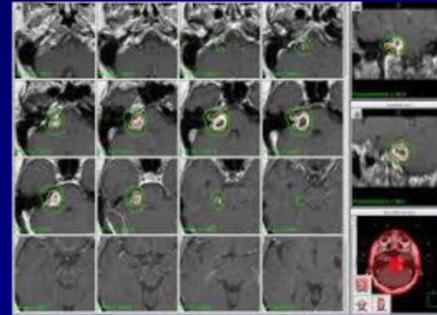
# Brachytherapy



# Stereotactic Radiosurgery

## Stereotactic Radiosurgery

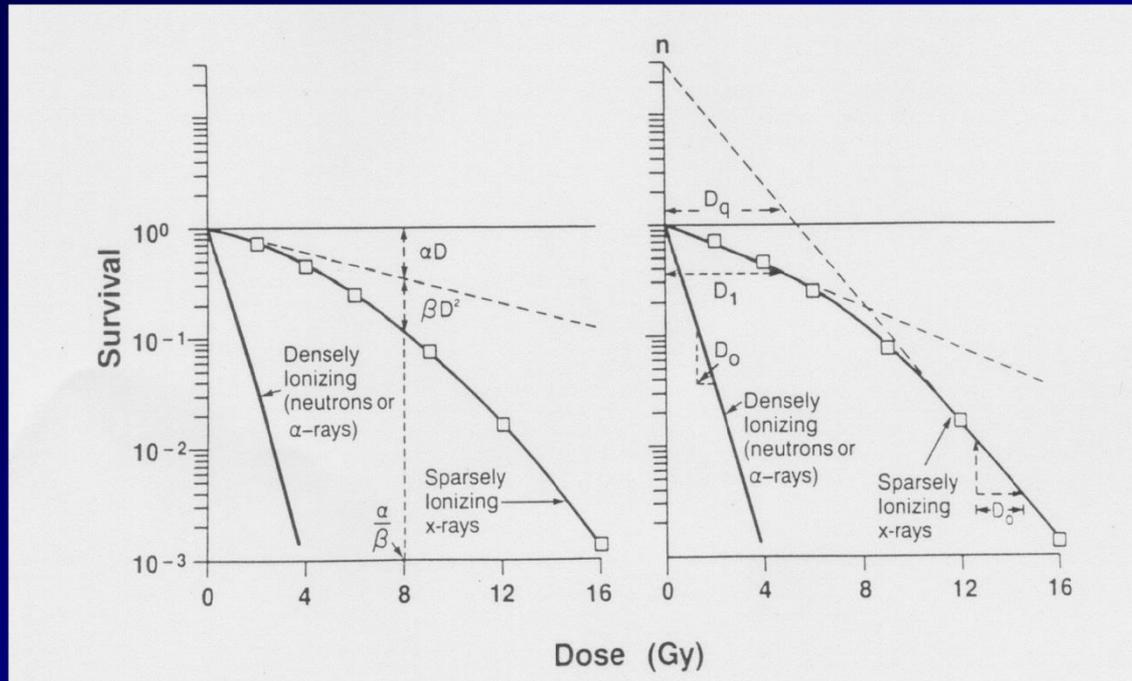
- Historically used to treat brain tumors (Gamma Knife)
- Technology has developed where we can now treat tumors in other body sites (Stereotactic Body Radiation Therapy)
  - Lung
  - Liver
  - Bone
- Cyber knife is a brand of machine that delivers stereotactic radiosurgery



# Radiation Biology

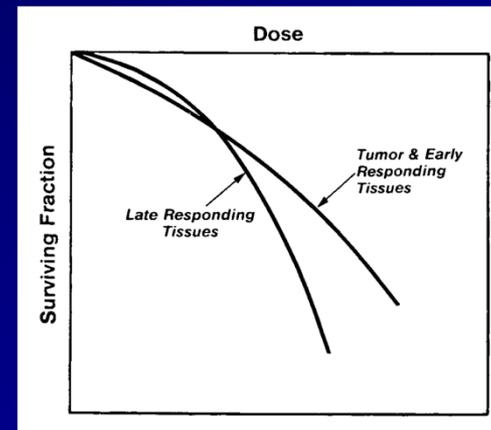
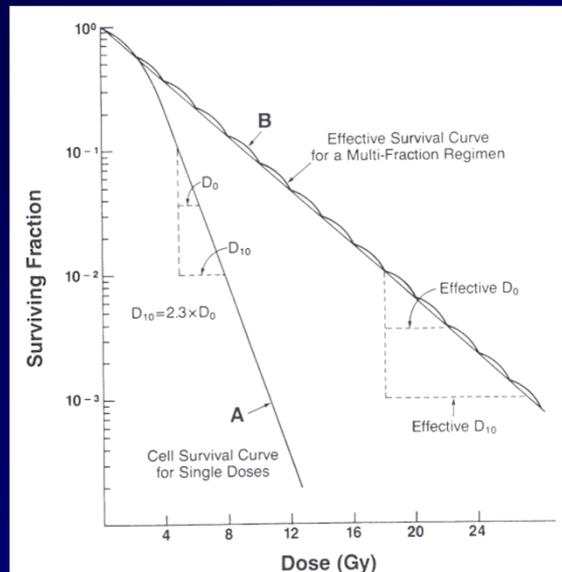
# Radiation Survival Curve

## Radiation survival curve



# Fractionation

## Fractionation



Rationale: take advantage of the slightly improved survival of normal tissue to smaller doses, amplified over many treatments

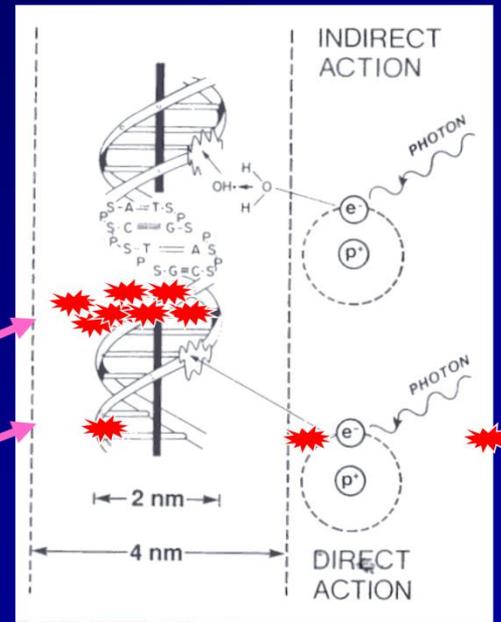
# The 4 “R”s of fractionated radiation

- Repair
  - Healthy cells repair DNA damage (so do tumor cells unfortunately)
- Reassortment (redistribution)
  - Radiation causes cells to accumulate in certain phases of the cell cycle
- Reoxygenation
  - Tumors reoxygenate after radiation
- Repopulation
  - Tumor and normal cells repopulate between doses of radiation

# Repair

## Repair

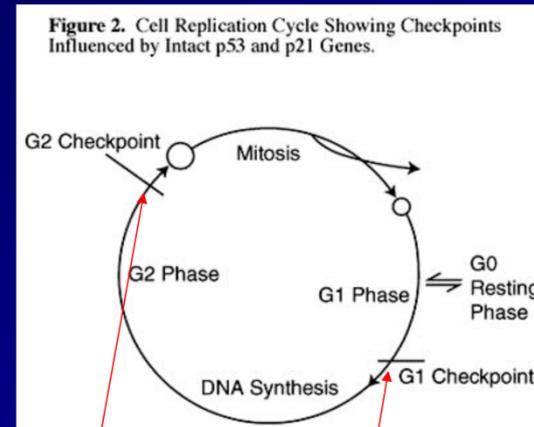
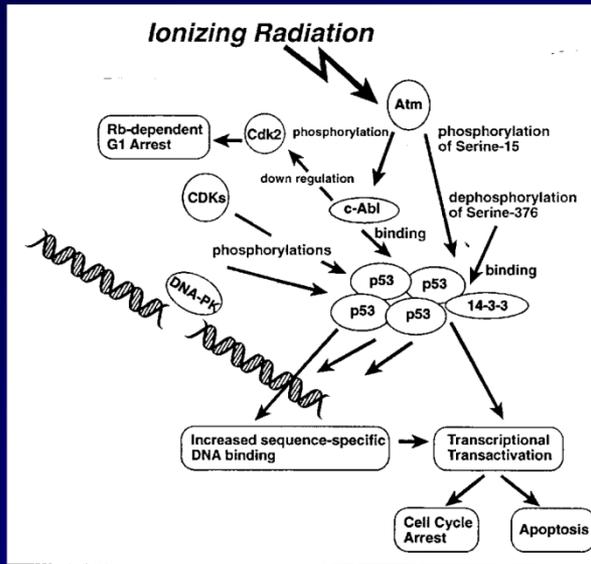
- DNA is the primary target of radiation
  - Indirect
  - Direct
  - SSB are repaired
  - DSB are key!
- Particles
- Photons



Cells that correct DNA dsb go on to divide another day.....REPAIR.

# Redistribution

## Redistribution

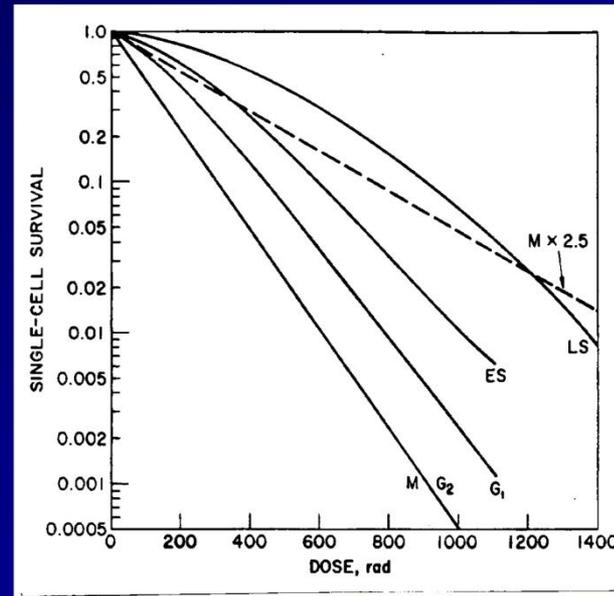
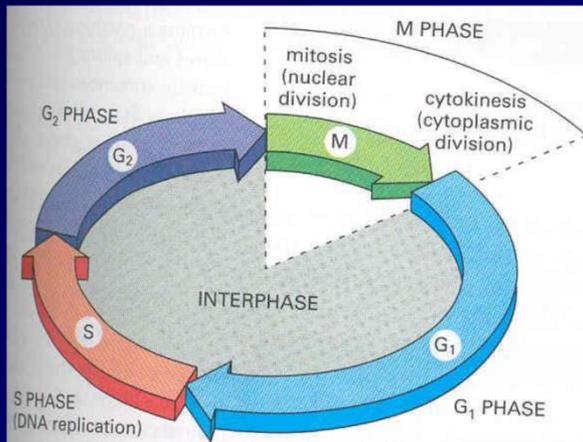


Accumulation in G1  
Accumulation in G2

Radiation induces cell cycle arrest to repair DNA damage.....REDISTRIBUTION

# Cell Cycle and Radiation Sensitivity

## Cell cycle and radiation sensitivity

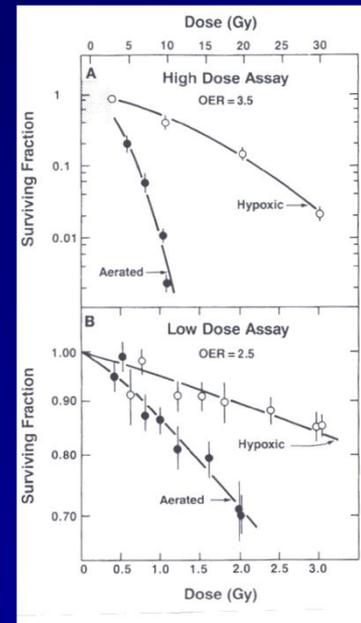
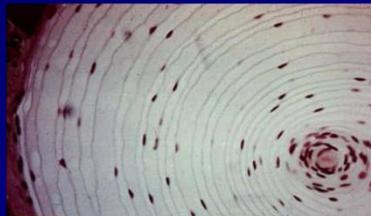
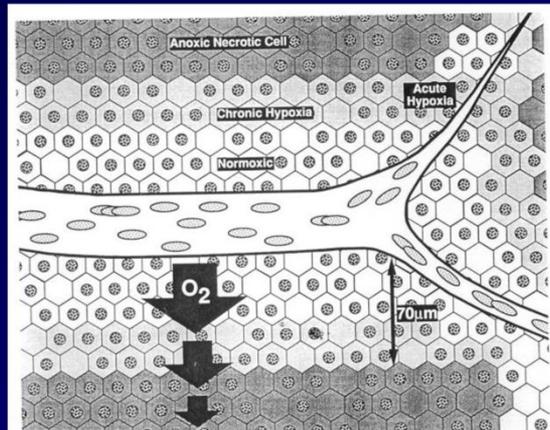


M > G<sub>2</sub> > ES > LS

Redistribution into a sensitive phase can matter!

# Reoxygenation

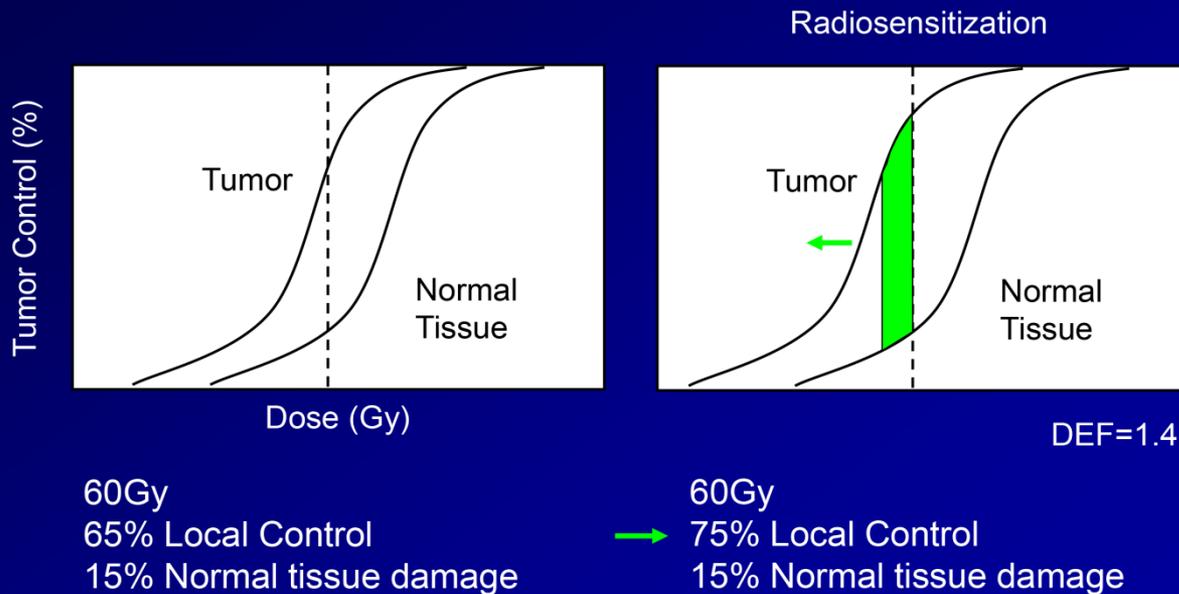
## Reoxygenation



Following radiation, tumors reoxygenate rapidly.....REOXYGENATION

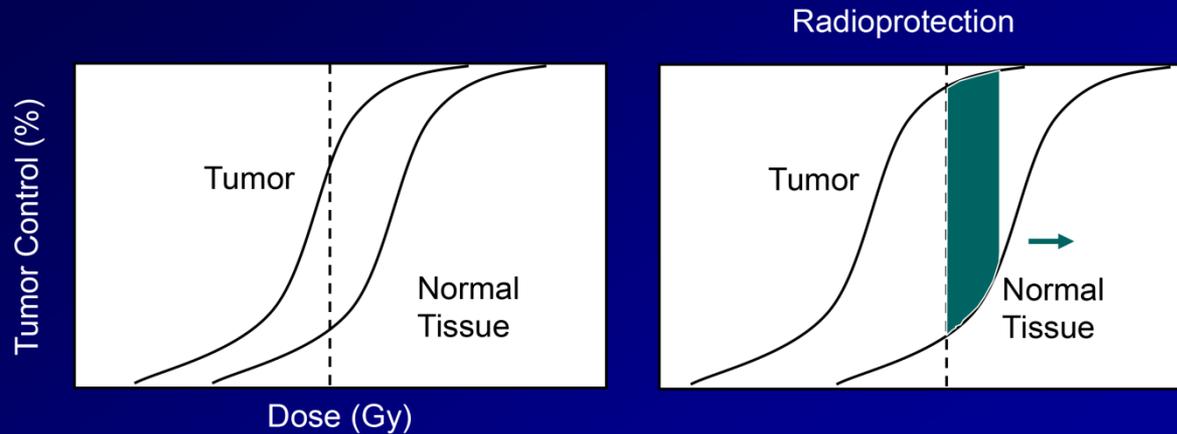
# Radiation Modifiers

## Radiation Modifiers



# Radiation Modifiers

## Radiation Modifiers



60Gy  
65% Local Control  
15% Normal tissue damage

70Gy  
75% Local Control  
15% Normal tissue damage

# Radiation Targets

- Single Target Agents
  - Growth factor receptors (EGFR, VEGFR)
  - DNA repair proteins (DNA-PK, Rad51)
  - Transcription factors (NFkB, p53)
  - Signal transduction proteins (Ras, PI3K, c-Abl)
- Multi-target Inhibition
  - Chaperone proteins (HSP90 inhibition)
  - Microenvironment (angiogenesis, vasculature)
  - Epigenetic modification
- Radiation Inducible Targets
  - Antigens or receptors (Fas, CEA)



# Issues for Target/Agent Development

- Mechanism
  - Cell type or condition specific
- Method of Targeting
  - Antibodies (EGFR, VEGFR)
  - Small molecules (Gleevec, Flavopiridol)
  - Gene therapy (TNFerade)
- Therapeutic ratio
  - Tumor > normal cells (Rad51)

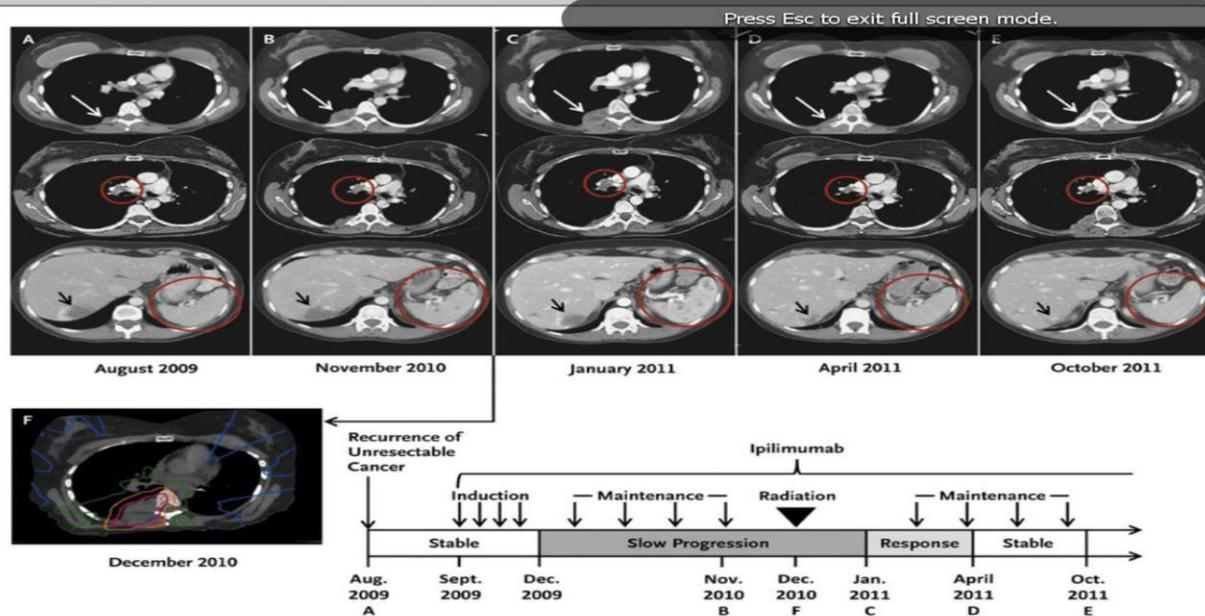
# Immunomodulatory agents

## Immunomodulatory Agents

- Can be combined well with RT
  - Abscopal effect
- Types of agents
  - PD1
  - PDL1
  - Others

# Abscopal Effect

# Abscopal Effect



**Figure 1. Results of Diagnostic and Radiotherapy Simulation Imaging throughout the Disease Course.**

Axial CT images are shown, corresponding to the timeline showing therapy and disease status. White arrows indicate the paraspinal mass, red circles indicate the right hilar lymphadenopathy and spleen, and black arrows indicate an incidental hepatic hemangioma. Panel A (top) represents the status before treatment with ipilimumab. Panel B shows enlargement of the paraspinal mass (top), stable right hilar lymphadenopathy (middle), and new splenic lesions (bottom). Panel C shows images 1 month after radiotherapy, when the response to radiotherapy had not yet occurred, with apparent continued worsening disease at all three sites. Several months after radiotherapy, the targeted paraspinal mass showed a response (Panel D, top). Furthermore, disease response outside of the radiation field was seen with decreased right hilar lymphadenopathy (middle) and resolution of splenic lesions (bottom). The response was durable, as shown in Panel E. Panel F shows the CT simulation image for radiotherapy planning, with the target volume (indicated in purple) encompassing the right paraspinal metastatic mass.

# Radiation Therapy

Clinical practice

# Goals of radiation therapy

- Cure
  - Cancer localized to one organ or region
- Palliation
  - Cancer disseminated to multiple organs that are causing bothersome symptoms

# Indications for radiation therapy

- Cure
  - Prostate cancer
  - Other urologic cancers
  - Breast cancer
  - Lung cancer
  - Head and Neck Cancer
  - Gynecologic Cancers
  - Pediatric Cancers
  - CNS tumors
  - Skin cancers
- Palliation
  - Bone pain
  - Shortness of breath
  - Neurologic symptoms
  - Pain from a space occupying lesion

# The Oncology Team

## The oncology team



# Develop a multimodality plan

- Surgery
- Radiation
- Systemic therapy
  - Chemotherapy
  - Targeted agents
- Other localized therapies
  - Focal ablation techniques
  - Focal drug delivery

# Treatment Process

## The radiation therapy treatment process

- Following consultation visit
- CT simulation (planning session)
- Transfer of images to treatment planning system
- Fusion of outside images

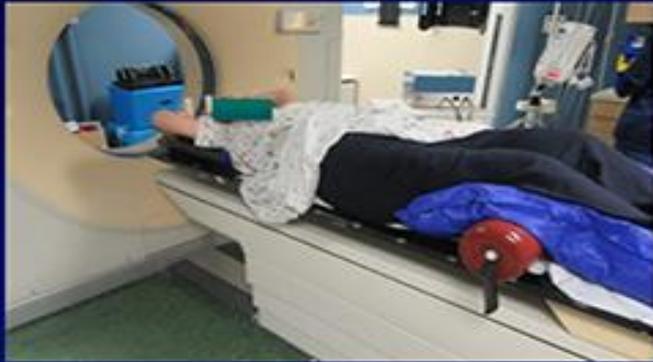


# CT

## CT simulation

- Wide bore CT present in all radiation oncology departments
- Flat table top (instead of curved)
- Immobilization devices created
- “Marks” placed on patient for alignment and treatment
- Ability to do 4D CT

# CT scan



# Radiation therapy process

## The radiation therapy treatment process

- Contouring (normal structures, target structures)
- Creation of plan (dosimetry)
- Evaluation of plan (by MD)
- Evaluation of plan (by physics)
- Transfer of plan to treatment machine
- Treatment delivery

# ROI Image

The screenshot displays a medical software interface for ROI (Region of Interest) management. The interface is divided into several sections:

- ROI Tools:** Includes 'POI Tools', 'Approval', and 'Fusion'.
- Current ROI:** Shows 'New ROI geometry' and 'CURRENT ROI'.
- Contouring:** Includes 'Brush', 'Smart contour', 'Spline', 'Polygon', and 'Freehand'.
- 3D Editing:** Includes 'Mode' (2D, 3D), 'Region growing', 'Deform', 'Translate', 'Rotate', 'Scale', 'Interpolate', 'Copy contour', 'Simpli', 'Paste contour', and 'Remo'.
- ROI List (Left Sidebar):**
  - ROI: External, CouchSurface, CouchInterior, CORD, BRSTEM, L COCHLEA, R COCHLEA, MANDIBLE, R PAROTID, L PAROTID, Post op bed, L neck, R neck, L neck PTV untrimmed, external - 0.3, R neck PTV untrimmed, L neck PTV trimmed, R neck PTV trimmed.
- Main Display:** Shows three views of a patient's head and neck CT scan with colored ROIs overlaid. The 2D axial view shows the cross-section of the head and neck. The 2D sagittal view shows the side profile of the head and neck. The 2D coronal view shows the front view of the head and neck.
- Status Bar:** Shows 'Primary image set: CT1 H&N 19OCT2015' and 'Secondary image set: -'. The date '10/23/2015' and time '1:44 PM' are also visible.

# Patient Presentations

# The treatment process – Patient A

- Develop a treatment plan (multimodality)
- Determine the appropriate RT modality
- Identify a target
- Identify surrounding normal tissue at risk
- Create a treatment plan (radiation)
- Deliver the treatment
- Follow the patient
- Returns to radiation oncology

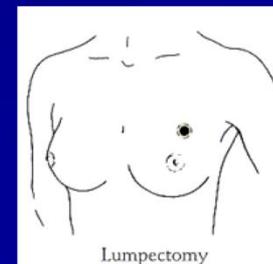
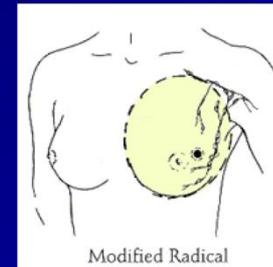
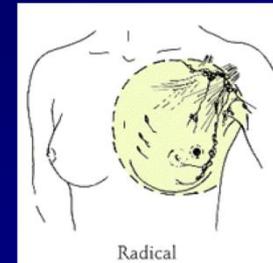
# Patient A

- 55 yo F with new lump in her left breast
- Suspicious abnormality on mammogram
- Biopsy consistent with infiltrating ductal carcinoma
- No family history of breast cancer

# Treatment Plan

## Develop a treatment plan

- Treatment options
  - Mastectomy
  - Breast Conserving Therapy (lumpectomy + RT)



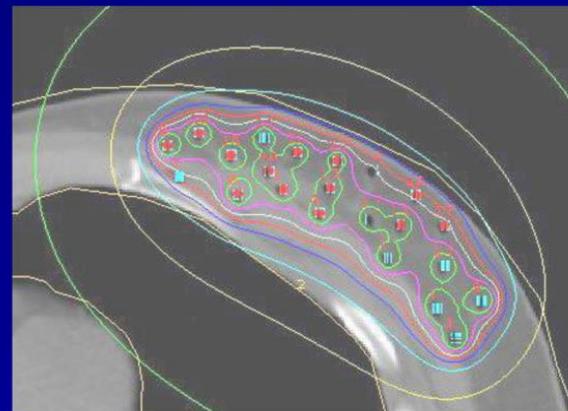
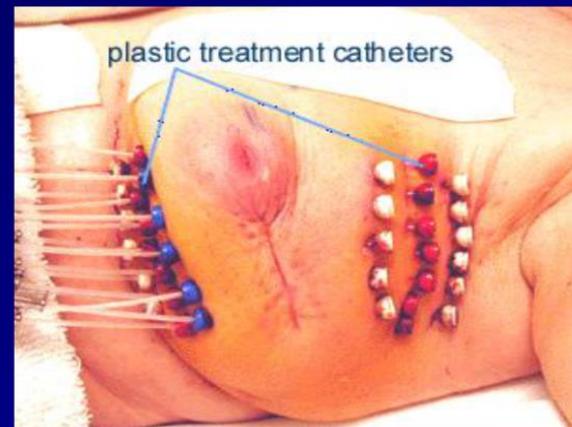
# Patient A

- Selects breast conservation
- Lumpectomy and sentinel lymph node biopsy
- Pathology reveals a 3 cm tumor and 4 axillary lymph nodes
- The patient receives chemotherapy

# Determine the RT Modality

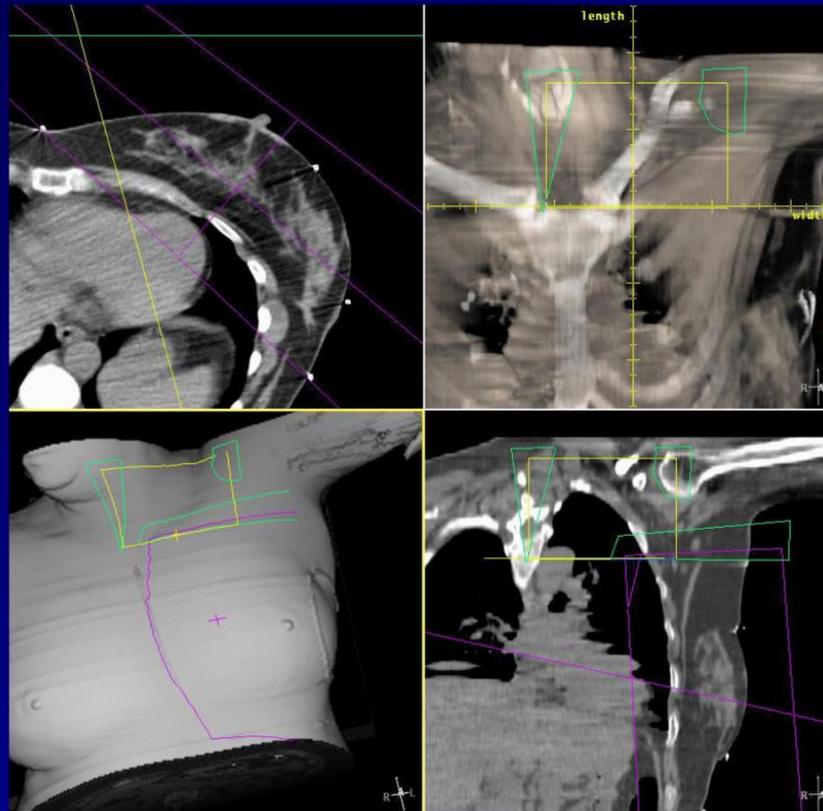
## Determine the RT modality

- External beam radiation
  - Protons
  - Photons
  - Electrons
- Brachytherapy
  - Sealed sources
  - Unsealed sources



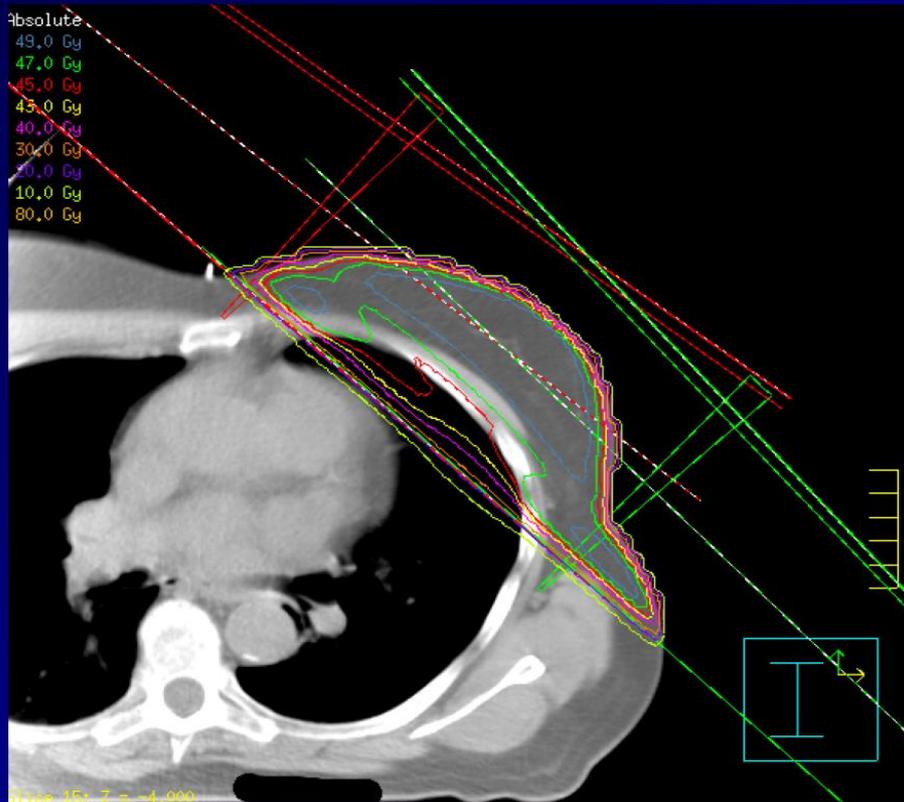
# Identify the target and normal tissue - Simulation

Identify the target and normal tissue - Simulation



# Create A Plan

## Create a plan



# Deliver The Treatment

Deliver the treatment



# Patient B

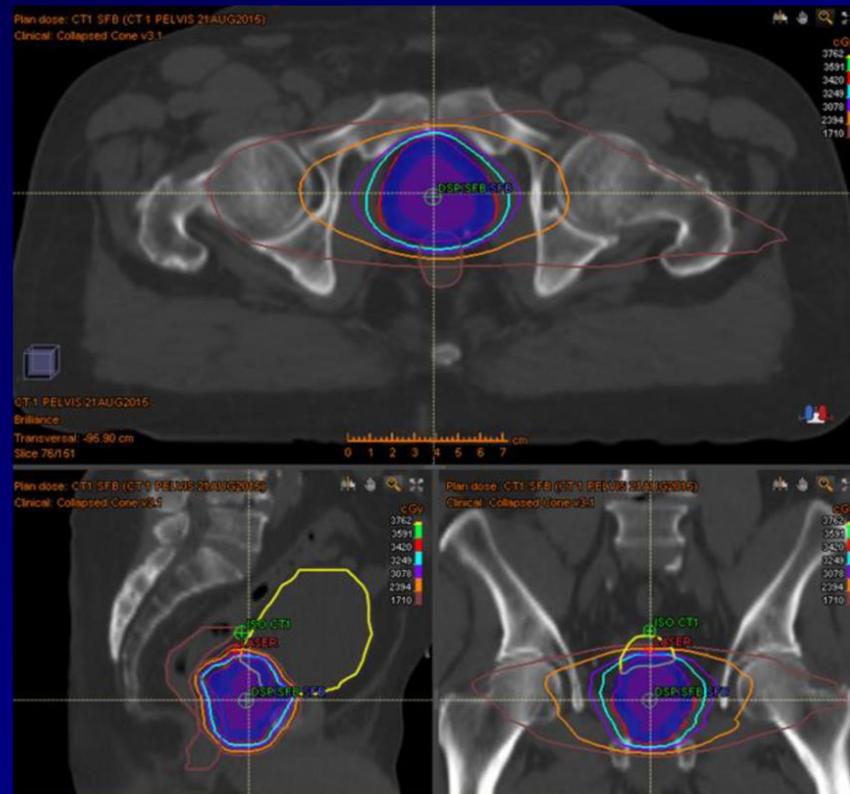
- Patient B
  - 54 yo M with an elevated PSA on routine exam
  - No prior medical problems
  - Biopsy consistent with adenocarcinoma of the prostate, Gleason score of 6

# Develop a treatment plan

- Surgery
- Surgery and radiation (based on surgical findings)
- Radiation
  - Brachytherapy
  - External beam RT
  - Combination
- Radiation and hormonal therapy

# Create A Plan

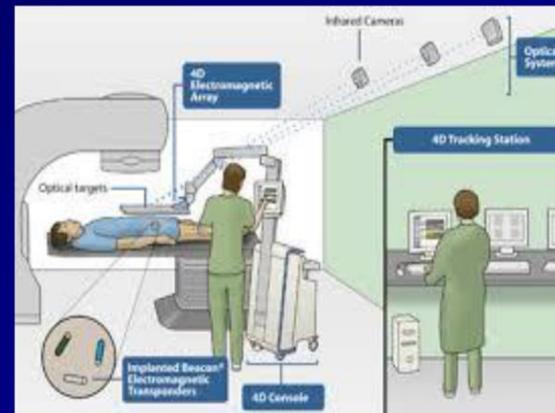
## Create a plan



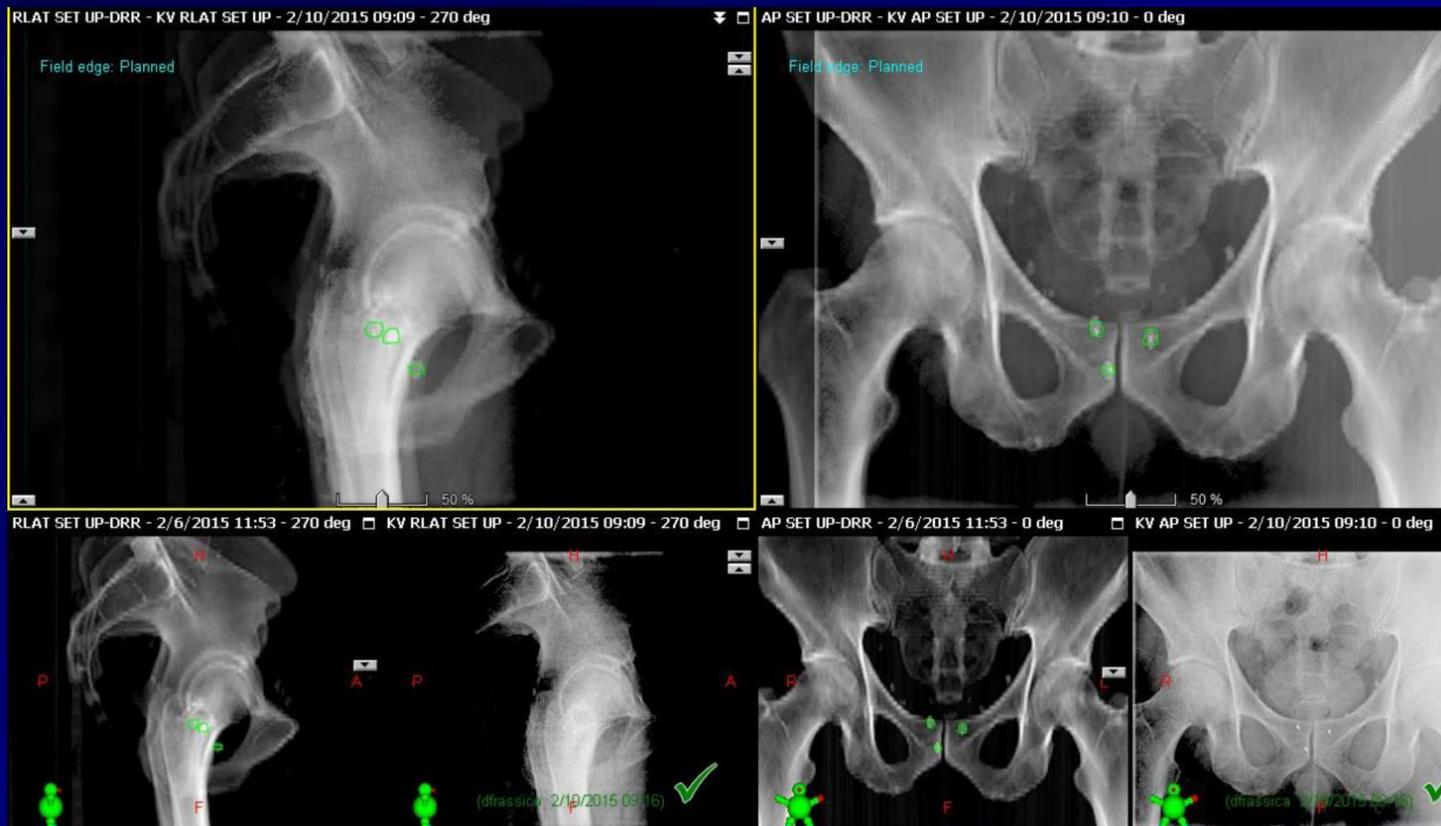
# Image Guided Radiation Therapy

## Image guided radiation therapy

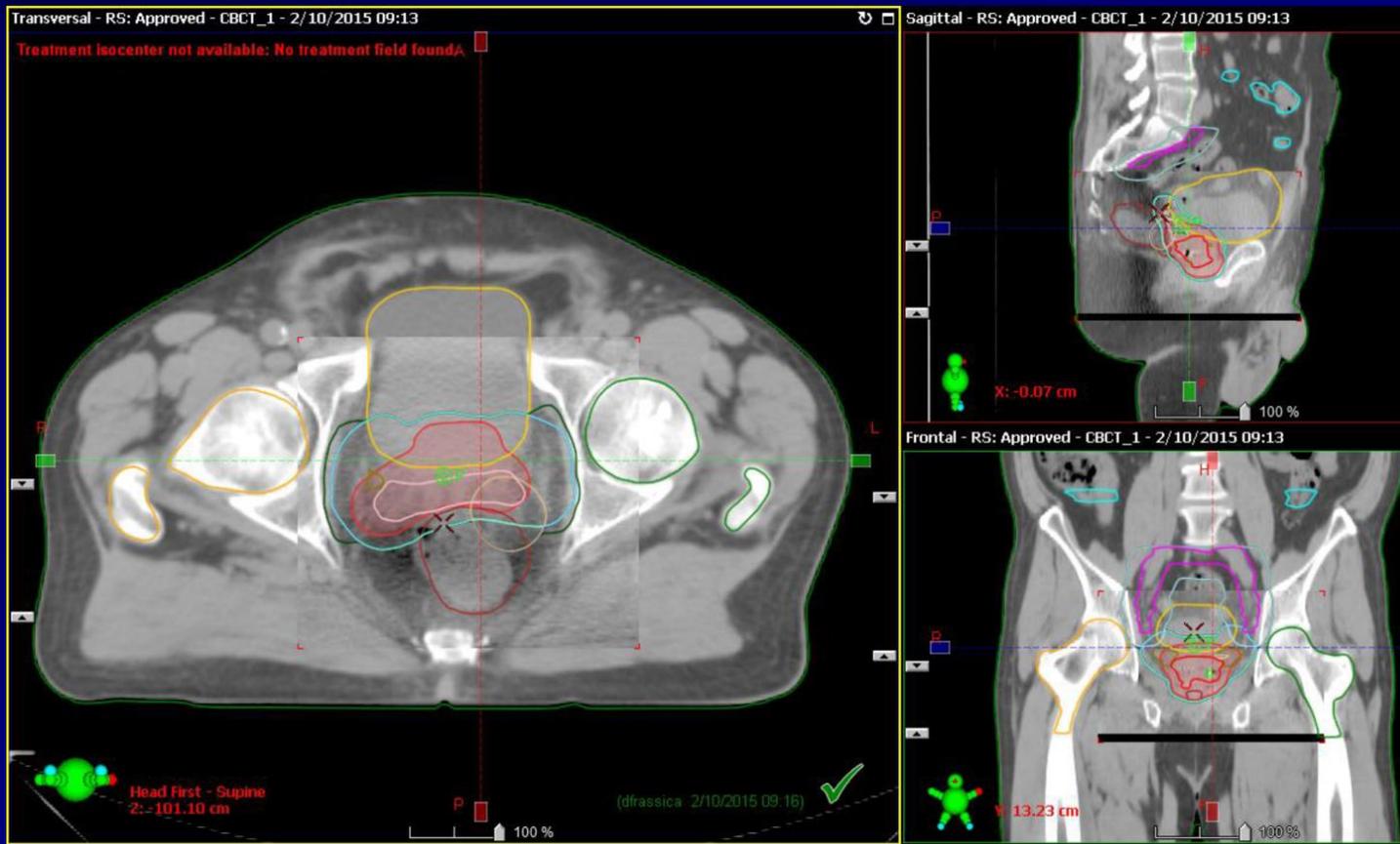
- Calypso
- Gold fiducial markers



# Image



# Image



# Deliver the Treatment

Deliver the treatment

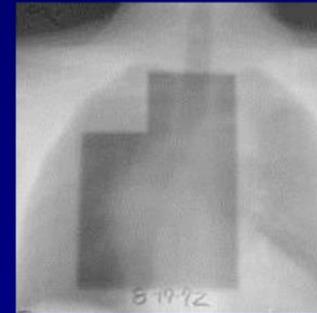
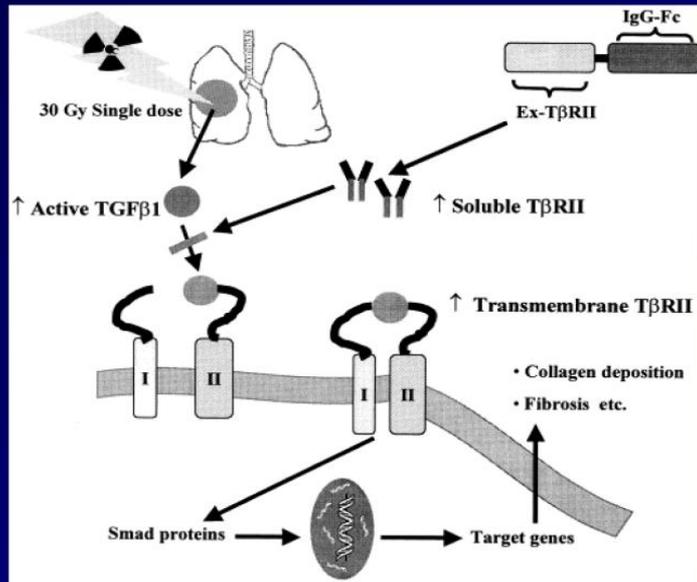


# Is it all just that easy?

- Normal tissue toxicity
  - Acute effects
  - Late effects
- Stem cell depletion, chronic oxidative damage, vascular destruction, fibrosis, and more
- Radiation is dosed to normal tissue, NOT tumor!

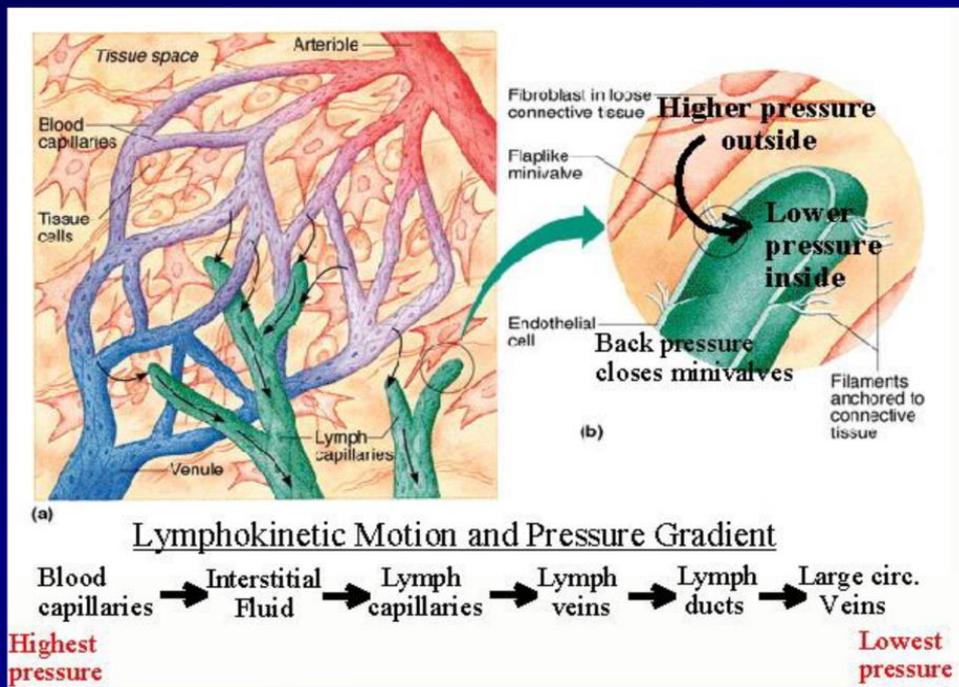
# Lung - Fibrosis

## Lung - Fibrosis



# Lymphedema

## Lymphedema – vessel damage



# Mucositis

Mucositis – stem cell depletion



# The future

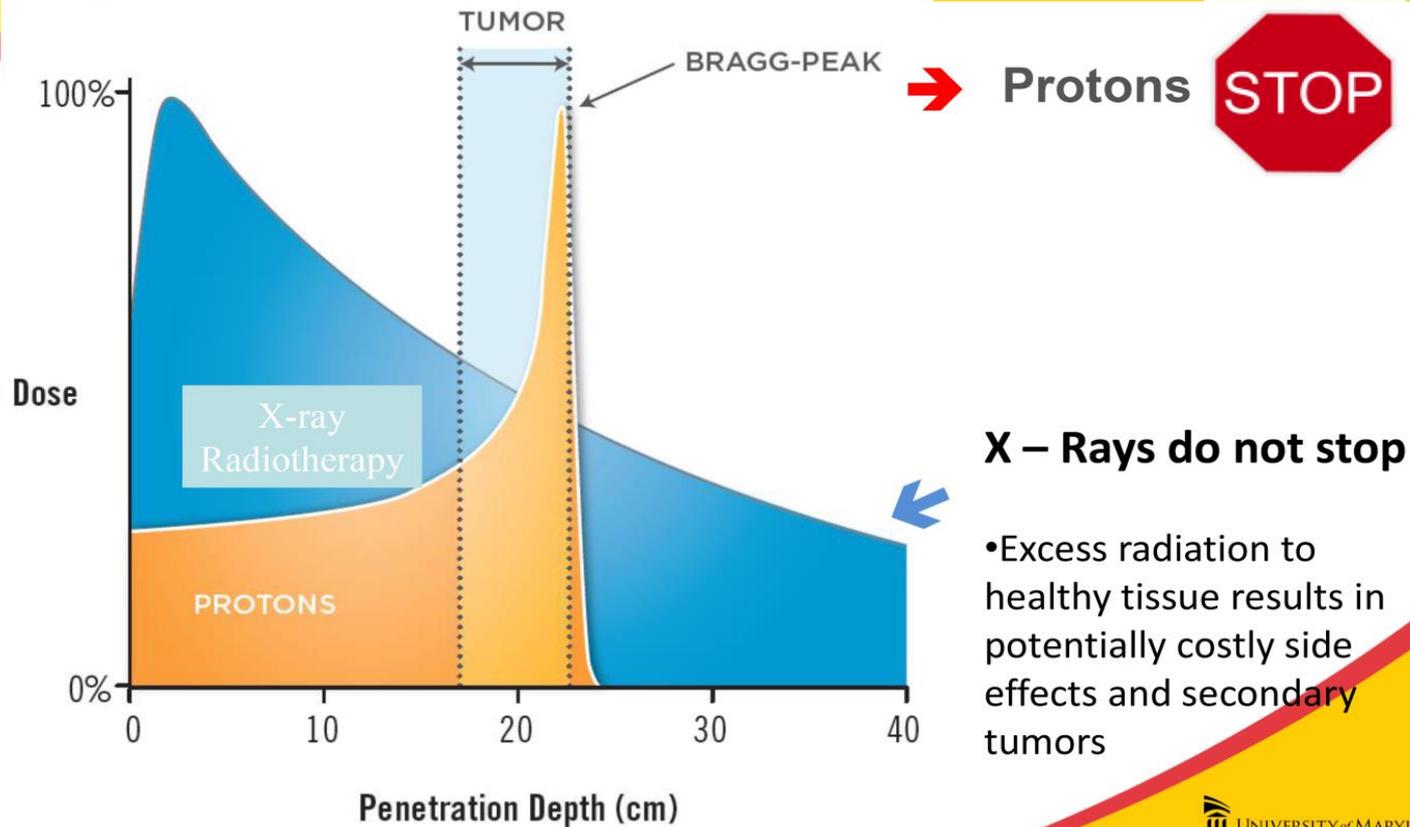
- Where do we go from here?

# The future of radiation

- Biology
  - Use radiation to induce targets for other agents
  - Better radiation sensitizers and protectors
  - Combining radiation and targeted drugs
- Physics
  - Improved targeting (imaging)
  - Improved delivery methods (equipment)
- Clinical
  - Translate exciting laboratory findings into the clinic
  - Continue to develop clinician-scientists

# Why Protons Can be Superior to Photons

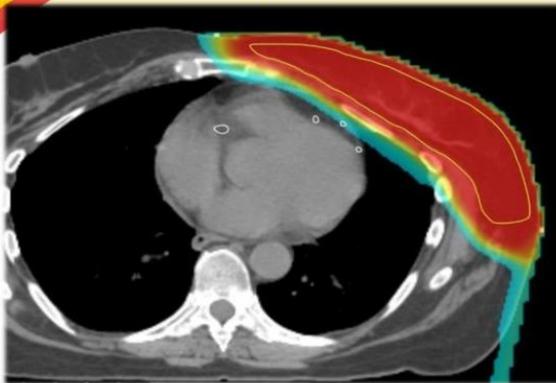
## Why Protons Can be Superior to Photons



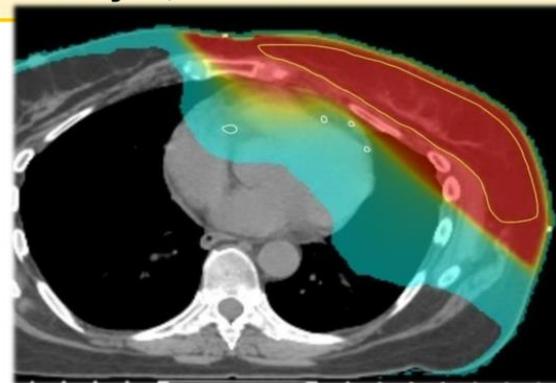
# Proton Therapy

*Proton Therapy Delivers Less Heart & Lung Dose*

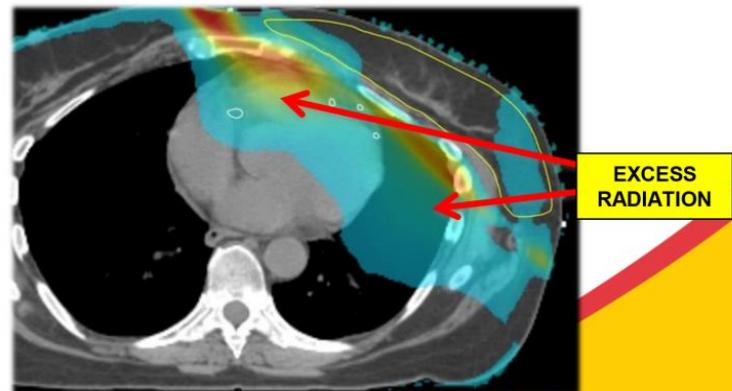
**Protons**



**X-Rays (Current Radiation Treatment)**



**X-Rays Minus Protons**



- **X-Rays Deliver Excess Radiation**
- **Resulting in**
  - **Coronary Artery Stenosis**
  - **Secondary Cancer**
  - **Lung Fibrosis**

# Maryland Proton Treatment Center

***Maryland Proton Treatment Center (MPTC) –  
A Regional Resource to Mid-Atlantic Healthcare Providers***



- \$200 million, 110,000 square feet, 5 treatment rooms, with unique patient thrupt process enhancing patient volume capacity allowing treatment of up to ~1900 patients/year (150-190 patients/day)

## **VISION**

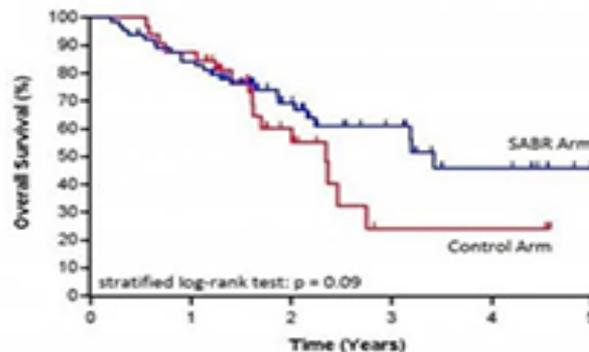
To become a Proton Center of Excellence across all academic missions,  
accessible to and in PARTNERSHIP with major regional Health system/Oncology providers

# Disease survival

## *Oligometastatic Disease*

- Stereotactic body radiation therapy delivered to oligometastatic disease improves overall survival!

### Results: Overall Survival



#### **Median Overall Survival**

Control Arm: 28 months  
(95% CI: 19-33 months)

SABR Arm: 41 months  
(95% CI: 26 months to 'not reached')

#### Number at risk:

Control	33	28	12	2	2	
SABR	66	53	29	15	7	1

# Future directions

## *Future Directions in Radiation Therapy*

- **Artificial Intelligence**
  - Automation of contouring and planning processes being evaluated
- **Continued development of combined therapies with radiation**
  - Chemotherapy/Systemic therapies
  - Other ablative therapies
  - Hyperthermia

# Message

## Take home messages

- Radiation is a tool used in cancer therapy
- Radiation causes DNA damage, which can lead to cell death
- The effects of radiation can be altered by modifying physical factors, physiologic factors, fractionation, drugs, and other variables
- Radiation can cause complications
- Radiation is INTERESTING!